REMARKS

The Advisory Action sent September 15, 2008 indicated the proposed amendments would not be entered for purposes of appeal. Accordingly, These proposed amendments are again submitted with this request for continued examination.

By this amendment, claim 1 is amended to clarify that the protein encoded by the nucleic acid portion designated "protein(Y)" is selected from the group consisting of mini-proinsulin and proinsulin. Claims 30-37 (similar to claims 1 and 6-12) are added as discussed below to explicitly recite "the hand of man" recite Claims 1, 6-12 and 27-37 are pending. Applicant respectfully submits that no issue of new matter arises. See comments under part 2) below.

Applicant gratefully acknowledges that only rejections under 35 USC §101 and 35 USC §112 (and one provisional rejection) remain to be overcome.

1) Rejections under 35 U.S.C. §112, first paragraph

Rejection of claims 1-3 and 6-12 was maintained under 35 U.S.C. §112, first paragraph as allegedly failing to meet written description and enablement requirements. Applicant respectfully traverses these rejections.

Written Description

The basis of this rejection appears to be that the claims do not recite "any functional characteristics". Office Action, page 4 line 18. The Office Action alleges that the claims recite a structure without any particular function. The Office Action recommends including language pertaining to functional characteristics of the genus. Applicant respectfully submits that such functional limitations are already present. Claim 1, paragraph 13 is also amended to more clearly indicate functionality. For example, claim 1, paragraphs 3 and 4, recite:

> the nucleic acid codes for a fusion protein comprising a peptide encoded by transport peptide linked via a peptide encoded by a first Z_1Z_2 to a protein encoded by said protein(Y) which is linked to T;

the peptide encoded by transport peptide improves the rate of secretion of the protein encoded by said protein(Y);

The nucleic acid has a recited function of coding for a fusion protein. Hirudin, encoded by the transport peptide, (see claim 1, paragraph 10) has a function of improving rate of secretion of mini-proinsulin or proinsulin, encoded by the nucleic acid fragment designated "protein Y". See, e.g., the specification page 2, lines 1 and 2: "Surprisingly, hirudin thus acts as a kind of enhancer peptide with respect to the yield of mini-proinsulin." Claim 1, thus as now written, clearly includes functional characteristics. The Examiner is respectfully requested to suggest any additional functional characteristics that might more fully describe the instantly claimed invention. Reconsideration and withdrawal of this rejection of claim 1 are respectfully requested.

Claims 6-12 and 27-29 ultimately depend from claim 1 and thus claim inventions that further limit the invention properly claimed in claim 1. Accordingly, reconsideration and withdrawal of this rejection of all claims are respectfully requested.

Enablement

The Office Action at page 5, lines 4 and 3 from bottom, states: "As stated above, applicants' recitation of 'transport peptide' is merely to indicate a variable component wherein many different peptides may be used." Applicant respectfully submits that indeed many hirudins including variants (encoded by "transport peptide") exist. See, for example, the paragraph bridging pages 5 and 6 of the specification. This limited set of transport peptides poses no requirement for undue experimentation and therefore is clearly enabled. See also the referenced application, DE 3 430 556. Accordingly, the genus of this claim element is clearly enabled in the art.

The Office Action acknowledges: "A person of skill in the art would most probably be able to make the claimed genus, but would not be able to determine whether each species will retain the specific intended function (this being especially worrisome since there are no functional limitations in the claim)."

Applicant respectfully submits that the enablement requirement has been characterized as relying on a test of whether "undue experimentation" would have been required. As discussed above and below, no undue experimentation is implicated for practicing the instantly

claimed invention. Applicant further respectfully submits that as described above, functional characteristics or limitations are features in the claims. This basis of rejection is thereby obviated or mooted.

As acknowledged in the Office Action no "undue experimentation" would be expected for the skilled artisan to make the claimed invention. The rejection must therefore rely on an allegation that the skilled artisan would require undue experimentation in order to use the claimed invention. The Office Action in this rejection, sheds light on the misapplication of the statute and caselaw. At page 6, line 4, the Office Action references an "undue burden". This will be interpreted by Applicant to mean "undue experimentation" since "undue burden" has no place in the applicable law.

The Action states: "Therefore the Examiner still believes that it is considered to be an undue burden for a person skill in the art to test all the possible constructs that are represented by the claimed structural formula." Applicant respectfully submits that claims recite a chemical construct and do not recite that all embodiments of the construct must be made. Nowhere does any claim require testing "all the possible constructs". According to 35 USC §112, the claimed invention must indeed be enabled. However, the enablement requirement pertains to each embodiment, the test being: Would undue experimentation be required for the skilled artisan to practice any one embodiment? (Inoperative embodiments are permitted so long as they may be discarded without undue experimentation.) In the present circumstance Applicant respectfully submits that for any one embodiment, only routine, not undue, experimentation would be required to practice the invention. As acknowledged above, "Making" is not an issue. To practice the invention, i.e., using the nucleic acid, the skilled artisan needs only routine laboratory practice to insert the nucleic acid into a host cell. Fermentation is also routine. See, for example, Example 4. Separation of protein components is also routine. See, for example, Example 6. If the skilled artisan is curious and wants to confirm benefits of practicing this invention, it would only be routine to construct a nucleic acid, for example without the "transport protein" component. Thus "improved rate of secretion" can be confirmed. Clearly no undue experimentation would have been required to practice the claimed invention.

The Office Action also includes another basis for this rejection: "There is no information in the claims or in the specification that would explain to a person skill in the art

as to which portion of the construct is essential for the intended function characteristics- and in a nutshell this is the Patent Offices' understanding of the 'structure-function relationship'." Applicant respectfully traverses this basis of rejection. For example, the structure of the nucleic acid segment "protein(Y)" has a function of encoding a protein selected from the group consisting of mini-proinsulin and proinsulin; the function of "transport peptide" is to encode hirudin or an hirudin variant; Px, Sx, Bn, Z, and R have known structures associated with their respective functions. For example, R, an arginine codon, by definition encodes for the amino acid, arginine. Its structure is obtainable from many molecular biology sources and is known to be, for RNA, aga, agg, cgu, cgc cga or cgg or the corresponding DNA codon. Such well known, structure-function relationships should not have to be repeated in every patent application. Accordingly, despite allegations to the contrary in the Office Action, a review of the specification and art unambiguously reveals that structure of the various claim elements is indeed correlated with understood function. Reconsideration and withdrawal of this aspect of the rejection are respectfully requested.

Claims 6-12 and 27-29 ultimately depend from claim 1 and thus claim inventions that further limit the invention claimed in claim 1. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

2) Rejection under 35 USC §101 - Non-Statutory Subject Matter

Claims 8, 11 and 12 were rejected as reciting non-statutory subject matter. Claims 8, 11 and 12 ultimately depend from claim 1 and thus "shall be construed to incorporate by reference all the limitations of the claim to which it refers." 35 USC §112, fourth paragraph.

The host cell of claim 8 comprises "the nucleic acid of claim 1 and thus incorporates "the hand of man" (February 19, 2008 Office Action, Page 4, line 4) as a limitation (incorporated by the reference to claim 1). Claims 11 and 12 depend from claims 6 and 7, respectively which each depend from claim 1. Thus the limitations of claim 1, including the "hand of man" are incorporated by reference in claims 11 and 12. Accordingly, the rejection of these claims is improper. Reconsideration and withdrawal of this rejection are respectfully requested.

Claim 30 is added to explicitly recite "An article of manufacture" to "clearly implicate the hand of man". The Advisory Action indicated that a 35 USC §112 type new matter rejection might be applied to this phrase (pending a new search and further consideration). See

"Continuation of 3." Applicants respectfully submit that no new matter rejection is proper. The hand of man is clear from the specification and manufacture is described in multiple places in the specification, for example at: Page 1, lines 23-29 ("Fusing" is a process of manufacture that produces the claimed article.) Page 4, lines 8 and 9 (Multicopy vectors and plasmids comprising "the above mentioned DNA molecule" (an article of manufacture) are disclosed.) Page 6, lines 4-7 (Stable integration is another process of manufacture.) Page 4, line 13 ("Recombinant DNA constructs", included in the scope of claim 1, are additional disclosure of articles of manufacture.) Page 6, lines 18 and 19 (Construction of yeast expression plasmid is disclosed – further evidence that applicant had an article of manufacture in possession at the time of invention.) Page 7, line 27 (A polymerase chain reaction is a process of manufacture.) Page 12, lines 8-14 (Preparing the protein includes "construction" of the expression cassette – further evidence of disclosure of a manufacturing process.) Clearly Applicant possessed the concept of an "article of manufacture" as a product of the invention inherent in these and other disclosures in the specification. Reconsideration and withdrawal of this rejection are accordingly respectfully requested.

Claims 31-37 that ultimately depend from claim 30 include this "hand of man" include by reference this recitation of the preamble. Accordingly, these claims clearly incorporate the "hand of man" by explicit reference. Since the "article of manufacture" recitation is asserted in the Advisory Action to require "new search and consideration". These claims are deemed to be patentably distinct from claims 1 and 6-12 which they parallel. These claims are supported by the existing claim set and parallel recitations of claims 6-12. No issue of new matter arises.

3) Provisional Double Patenting Rejections

Claim 1 was provisionally rejected under a judicially created concept of double patenting. If still proper, Applicant will take appropriate action, such as an amendment or other action in this or 10/076,634 if and when claims are finalized by indication of allowable claimed subject matter.

Conclusion

In view of the above amendments and remarks, Applicant respectfully requests reconsideration and withdrawal of all pending rejections. Applicant respectfully submits that the application is now in condition for allowance and request prompt issuance of a Notice of

Allowance. Should the Examiner believe that anything further is desirable that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

Fees

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

Respectfully submitted,

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